Bandolier 139

Independent evidence-based thinking about health care

Déjà vu all over again

Bandolier seems to have spent much of the last decade or so urging caution on people who want to rush through major changes on the basis of some new "evidence". One points out that "new" and "evidence" in the same sentence is an unlikely and sometimes unfortunate pairing, but one is told off as being an old fool.

While that might be an excellent and accurate description for many reasons, this isn't necessarily one of them. We have learned, often painfully, that the requirements of evidence are not easily come by, and that it is all too easy to be misled. It is therefore comforting, at least to Bandolier, to see a brace of fine papers from Greece, extolling the philosophy of caution in the face of the popular. Just because wisdom is received, often just through repetition, that doesn't make it right. If we want to be right we need good evidence, and we need to look at the totality of evidence.

Toss of a coin

Bandolier well remembers speaking with a Medical Director of an organisation who espoused the opinion that evidence from a trial of 20 patients with statistical significance at the 5% level was sufficient evidence to make a change in policy. The chances of any such evidence being right, or at least strong, is about 10 to 1 against or worse.

Watered wine

These papers underscore our need to reduce the amount of dross in the medical literature, and, rather, concentrate on doing fewer but better studies on what is important. That is easier said than done, given the vagaries of finding cash or other resources to support research. We need stronger stuff than the watered wine so often put before us. Yes, there is some good stuff in the literature, but one might argue that good evidence in the medical literature is as rare as having an active ingredient in a homeopathic medicine.

In this issue

On caution

There are many traps and pitfalls to negotiate when assessing evidence, and it is all too easy to be misled by an apparently beautiful study that later turns out to be wrong, or by a meta-analysis with impeccable credentials that seems to be trying to pull the wool over our eyes. Although these are themes often found in the pages of Bandolier, a little reinforcement rarely comes amiss.

Law of initial results

So often early promising results are followed by others that are less impressive. It is almost as if there is a law that states that first results are always spectacular, and subsequent ones are mediocre: the law of initial results. It now seems [1], that there may be some truth in this.

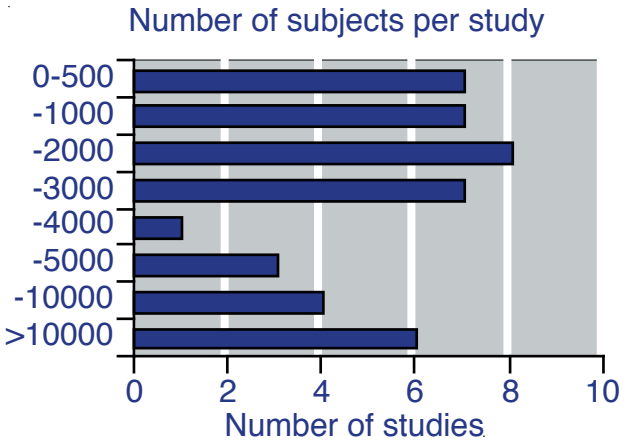
Study

Three major general medical journals (New England Journal of Medicine, JAMA, and Lancet) were searched for studies with more than 1000 citations published between 1990 and 2003. This is an extraordinarily high number of citations when you think that most papers are cited once if at all, and that a citation of more than a few hundred times is as rare as hens' teeth.

Results

Of the 115 articles published, 49 were eligible for the study because they were reports of original clinical research (like tamoxifen for breast cancer prevention, or stent versus balloon angioplasty). Studies had sample sizes as low as 9 (nine) and as high as 87,000. There were two case series and four cohort studies, and 43 randomised trials. The randomised

Figure 1: Size of highly-cited RCTs



trials were very varied in size, though, from 146 to 29,133 subjects (median 1817 subjects; Figure 1). Fourteen of the 43 randomised trials (33%) had fewer than 1000 patients and 25 (58%) had fewer than 2,500 patients.

Of the 49 studies, seven were contradicted by later research. These seven contradicted studies included one case series with 9 patients, three cohort studies with 40,000 to 80,000 patients, and three randomised trials, with 200, 875 and 2002 patients respectively. So only three of 43 randomised trials were contradicted (7%), compared with half the case series and 3/4 cohort studies.

A further seven studies found effects stronger than subsequent research. One of these was a cohort study with 800 patients. The other six were randomised trials, four with fewer than 1000 patients and two with about 1500 patients.

Most of the observational studies had been contradicted, or subsequent research had shown substantially smaller effects, but most randomised studies had results that had not been challenged. Of the nine randomised trials that were challenged, six had fewer than 1000 patients, and all had fewer than 2003 patients. Of 23 randomised trials with 2002 patients or fewer, 9 were contradicted or challenged. None of the 20 randomised studies with more than 2003 patients were challenged.

Most published research false?

In the past people have commented that only 1% of articles in scientific journals are scientifically sound [2]. Bandolier has often examined articles showing how we consumers of scientific literature can be misled, and how we often are. Another paper from Greece [3] is replete with Greek mathematical symbols and philosophy. It makes a number of important points:

1 The smaller the studies conducted in a scientific field, the less likely the research findings are to be true.
2 The smaller the effect sizes in a scientific field, the less likely the research findings are to be true.
3 The greater the number and the fewer the selection of tested relationships in a scientific field, the less likely the research findings are to be true.
4 The greater the flexibility in designs, definitions, outcomes, and analytical modes in a scientific field, the less likely the research findings are to be true.
5 The greater the financial and other interests and prejudices in a scientific field, the less likely the research findings are to be true.
6 The hotter a scientific field (the more scientific teams involved), the less likely the research findings are to be true.

Ioannides [3] then performs a pile of calculations and simulations but then demonstrates the likelihood of us getting at the truth from different typical study types (Table 1). This ranges from odds of 2:1 on (67% likely to be true) from a systematic review of good quality randomised trials, to 1:3 against (25% likely to be true) from a systematic review of small inconclusive randomised trials, to even lower levels for other architectures.

Comment

There is lots more in these fascinating papers, but from here on in it all gets more detailed and more complex without becoming necessarily much easier to understand. There is nothing here that contradicts what we already know, namely that if we accept evidence of poor quality, without validity, or where there are few events or numbers of patients, we are likely, often highly likely, to be misled.

If we concentrate on evidence of high quality, which is valid, and with large numbers, that will hardly ever happen. As Ioannidis also comments, if instead of chasing some ephemeral statistical significance we concentrate our efforts where there is good prior evidence, our chances of getting the true result are better - concentrating on all the evidence. Which may be why clinical trials on pharmaceuticals are so often significant statistically, and in the direction of supporting a drug. Yet even in that very special circumstance, where so much treasure is expended, years of work with positive results can come to naught when the big trials are done and do not produce the expected answer.

References:

1 JPA Ioannides. Contradicted and initially stronger effects in highly cited clinical research. JAMA 2005: 294: 218-228.
2 R Smith quoting Prof D Eddy, BMJ 1991 303: 798-799.
3 JPA Ioannides. Why most published research findings are false. PLoS Medicine 2005 2: e124. (www.plosmedicine.org)

Table 1: Likelihood of truth of research findings from various typical study architectures

Example	Ratio of true to not true	Positive predictive value
Confirmatory meta-analysis of good quality RCTs	2:1	0.85
Adequately powered RCT with little bias and 1:1 pre-study odds	1:1	0.83
Meta-analysis of small, inconclusive studies	1:3	0.41
Underpowered, but poorly performed phase I/II RCT	1:5	0.23
Underpowered, but well performed phase I/II RCT	1:5	0.17
Adequately powered exploratory epidemiological study	1:10	0.2
Underpowered exploratory epidemiological study	1:10	0.12
Discovery-orientated exploratory research with massive testing	1:1,000	0.001

Schizophrenia and suicide

Schizophrenia is associated with a significant risk of suicide. Two systematic reviews provide an insight into the level of risk, and into the risk factors involved.

Suicide risk in schizophrenia [1]

A systematic review used a literature search for articles observing cohorts of schizophrenic patients with at least two years of observation and at least 90% follow up. Searching involved two electronic databases (one a specialist psychiatric database), plus extensive bibliographic and reference reviews over 90 years. Studies selected used diagnostic criteria of their times for schizophrenia.

From each of about 60 studies information was collected on number of patients, deaths, suicides, and length of follow up.

Results

Twenty-nine cohorts observed schizophrenics from date of admission or illness onset, and another 32 were composed of any type of patient. The studies were as small as a few tens of patients, to over 9,000. Most involved several hundred patients, followed up for two to 22 years.

For those studies that examined patients from first admission or new onset (22,598 patients), the case fatality estimate (percentage of original sample who died by suicide) was 2.9% (95% CI 4.3 to 5.6%). Of all deaths, 31% were deaths by suicide. Among studies using mixed samples (25,578 patients), the case fatality estimate was 2.3% (1.5 to 3.5%) and 6% of the all deaths was by suicide.

Analysis according to time of follow up suggested that suicide risk was greater sooner rather than later after diagnosis or onset. The estimate of lifetime suicide prevalence in those observed from first admission or illness onset was 5.6% (95% confidence interval, 3.7% to 8.5%). Mixed samples showed a rate of 1.8% (95%CI, 1.4% to 2.3%). Case fatality rates showed no significant differences when studies of patients diagnosed with the use of newer criteria were compared with studies of patients diagnosed under older criteria.

Risk factors for suicide in schizophrenia [2]

A second systematic review used a broad search strategy to select studies with information about risk factors for schizophrenia. For inclusion, studies were required to have a patient diagnosis of schizophrenia and related disorders, have more than 90% of patients aged over 16 years, be cohort studies with a minimum follow up period of one year, or be a case-control study, investigating specific risk factors.

These risk factors included sociodemographic information, family history (particularly of psychiatric disorders, depression, suicide or alcohol misuse), personal history (broken home, parental loss, education, IQ, recent loss), and clinical history. The clinical history factors were widely drawn, and included factors like psychiatric symptoms (depression, fear of mental disintegration), suicide ideation, previous suicide attempts, and many others.

Table 1: Factors with limited or no association with suicide in schizophrenia

Factor with limited association with suicide	
Male gender	Worthlessness
Living alone	Hopelessness
Not living with family	Impulsivity
Family history of depression	
Factor not associated with suicide	
Ethnicity	Violence
Married	Physical illness
Divorced	Alcohol misuse
Single	Negative symptoms
Having children	Social withdrawal
Employed	Sleep disturbance
Unemployed	Insight
Broken home	Delusions
Limited education	Hallucinations: command
Higher education	Compulsory admission
Living with family	Recent suicide threat
Family history of suicide	Positive symptoms
Family history of psychiatric disorder	
Family history of alcohol misuse	
Substance misuse or dependence	

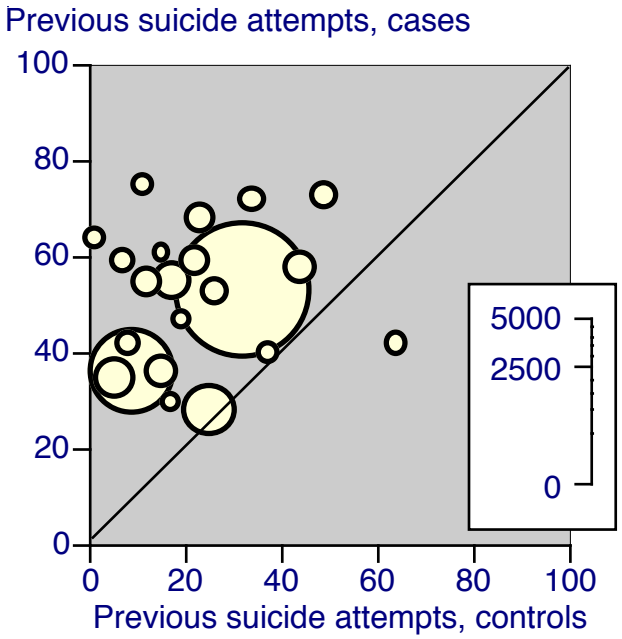
Results

In all, 29 studies were included, three prospective cohorts, two retrospective cohorts, three nested case control studies, fourteen case control studies with similar controls, and seven case control studies with different or unclear controls. In total, there were 1675 suicides (average 58 per study, median 33) and 11,303 controls (average 390 per study, median 69). Most of the studies specified a diagnostic criterion for schizophrenia.

The nature of the controls chosen varied widely. Some were randomly selected inpatients or outpatients from the same institution, some were surviving patients from the same cohort from whom the suicide cases were taken, or selected from non-suicide inpatients, or patients with a high risk of suicide.

A number of risk factors were not associated more often with suicide cases than controls (Table 1), or associated statistically, but not robustly because of the small number of studies and patients. A number of other factors were robustly associated with suicide, either because there were larger numbers of studies and patients, or because there was a large effect with moderate numbers of studies and patients (Table 2). An example of consistency between studies relating past attempts of suicide is shown in Figure 1.

Figure 1: Previous suicide attempts in schizophrenic patients committing suicide, and controls



Recent suicide ideation, fear of mental disintegration, drug misuse or dependence, recent depression, recent loss, poor compliance with treatment, and history of suicide attempt all occurred much more often with suicide cases than with controls (Table 2, which has odds ratios from the paper as well as the more useful relative risk). Hallucination was the only factor that occurred less frequently.

Comment

About 1 in 20 schizophrenics will commit suicide during their lifetimes, more often near illness onset. The findings of the meta-analysis do seem to be borne out by other studies published since the meta-analysis was completed. For instance, there were 78 completed suicides in 4237 acute inpatients with schizophrenia admitted between 1985 and 2000 in Taiwan [3]. That is a rate of 2%, and half of the suicides occurred within four years of first admission, but Taiwan may well have lower rates of some important risk factors, particularly drug misuse. Rates of suicide in mainland China [4] in the late 1990s averaged 0.7% of the schizophrenic population annually (28,737 suicides in people with schizophrenia out of 4.25 million people with schizophrenia in China). If half of the suicides were in the first few years, that would equate to a lifetime risk of almost 6%. These two large studies in east Asia confirm the overall estimate of between 2% and 5% lifetime risk of death by suicide.

A number of factors, particularly recent suicide ideation, fear of the impact of the illness on mental functioning, and depression, are positively associated with increased risk of suicide in patients who have schizophrenia. The nature of the disorder seems less important. Active treatment of affective symptoms, improving adherence to treatment, and maintaining vigilance in patients with risk factors may contribute to reducing actual suicides in patients with schizophrenia. These are two important systematic reviews.

The interesting thing about the mainland China study of suicide [4] was that it examined suicide by schizophrenic patients as a percentage of all suicides. Ten percent of all suicides were suicides by schizophrenic patients. This implies that recognising suicidal risk factors in patients with schizophrenia should be a major factor in reducing deaths from suicide.

References:

1 BA Palmer et al. The lifetime risk of suicide in schizophrenia. Archives of General Psychiatry 2005 62: 247-252.
2 K Hawton et al. Schizophrenia and suicide: systematic review of risk factors. British Journal of Psychiatry 2005 187: 9-20.
3 CJ Kuo et al. Risk factors for completed suicide in schizophrenia. Journal of Clinical Psychiatry 2005 66: 579-585.
4 MR Phillips et al. Suicide and the unique prevalence pattern of schizophrenia in mainland China: a retrospective observational study. Lancet 2004 364: 1062-1068.

Table 2: Factors associated with successful suicide in patients with schizophrenia

Risk factor	Number of			Risk factor (%) in		Relative risk (95% CI)	Odds ratio (95% CI)
	Trials	Patients	Events	Cases	Controls		
Recent suicide ideation	4	486	142	52	4	12 (6.3 to 23)	30 (12 to 73)
Fear of mental disintegration	4	362	55	33	4	5.9 (3.1 to 11)	12 (1.8 to 81)
Drug misuse or dependence	4	3385	240	22	6	2.6 (1.8 to 3.9)	3.2 (2.0 to 5.2)
Recent depression	7	653	178	42	16	2.3 (1.8 to 3.0)	6.2 (1.3 to 30)
Recent loss	3	317	110	43	31	2.3 (1.6 to 3.2)	4.0 (1.4 to 12)
History of suicide attempt	22	6849	1952	53	25	2.2 (2.0 to 2.4)	4.1 (2.8 to 6.0)
Past depression	9	2336	599	44	21	2.2 (1.8 to 2.7)	3.0 (2.1 to 4.5)
Poor compliance with treatment	4	363	122	54	20	2.0 (1.5 to 2.7)	3.8 (2.2 to 6.4)
Past ideation	4	1532	339	52	19	1.7 (1.4 to 2.1	3.3 (1.8 to 6.4)
Agitation or motor restlessness	4	1470	284	50	17	1.3 (1.04 to 1.7)	2.6 (1.5 to 4.4)
Hallucination	6	2133	961	32	47	0.7 (0.6 to 0.8)	0.5 (0.4 to 0.7)

Incidence of dementia

Differences in dementia incidence and prevalence in older people around the world are believed to be related to vascular risk. Because different studies use different diagnostic criteria in different populations, comparisons between them are of limited value in relating development of dementia to underlying health problems. Bandolier 48 looked at a comparison of different diagnostic criteria applied by the same people to a large cohort of older people with full clinical and neuropsychological examination. That study showed that the diagnosis of dementia in the same population ranged from 3% to 30%.

In order properly to examine issues of underlying health and their relation to dementia, different populations have to be examined using the same diagnostic criteria applied in the same way. A large UK MRC study has done that [1].

Study

The study was carried out in five areas around the UK. Two (Gwynedd, Newcastle) had higher rates of angina, intermittent claudication, heart attacks, and stroke. Cambridgeshire and Oxford had lower rates, and Nottingham was intermediate. Population samples were drawn from health authority lists, with random selection to recruit at least 1,250 individuals in each centre in the age groups 65-74 years, and 75 years and above.

After an initial screening interview, there was a more intensive assessment of a subsample of the population. After two years, there was a rescreen of individuals not selected for assessment at baseline, followed by a further assessment sample. Interviewers were trained to use standard formats, with considerable effort made to ensure ongoing comparability locally and across all sites. The interview lasted about an hour and contained basic information plus a variety of instruments related to dementia. Diagnosis of dementia was based on DSM-III, with clinical judgement for those unable to complete the interview.

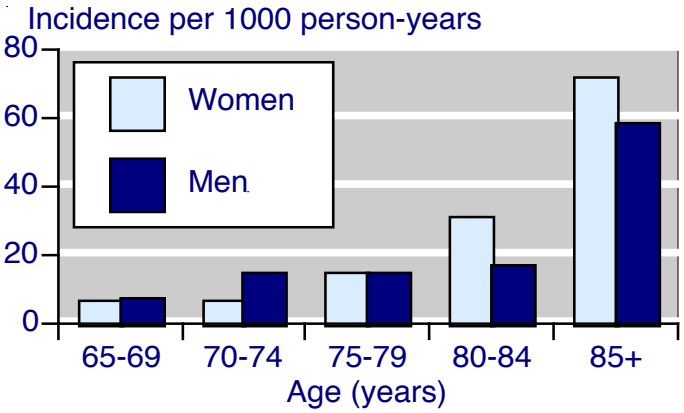
Essentially the incidence rate was calculated as the proportion of people with incident dementia, divided by two years, and presented as a rate per 1,000 person-years.

Results

As with other studies, incidence of dementia increased with age for women and men (Figure 1). Incidence was about 10 per 1,000 person-years (about 1% of the age group) in men and women between age 70 and 80 years, with rates increasing to about 60 per 1,000 person-years (about 6%) in those aged 85 years and older. There was no indication that rates did not continue to increase in the oldest old.

Although individual sites differed considerably in rates of vascular disease, there was no indication of a lower incidence in sites with the lower rates of vascular disease (Figure 2). Extrapolation to the population of England and Wales indicated that there would be about 180,000 new dementia cases occurring each year.

Figure 1: Incidence of dementia by age in women and men



Comment

This is a complex and detailed study that performed a number of sensitivity analyses and examined various issues of methodology. Its findings were broadly in line with others in Europe, Asia, and the USA. Its value was that it indicates that there is no apparent link between vascular health and dementia, and confirmed that rates do not level off or decline in the oldest old.

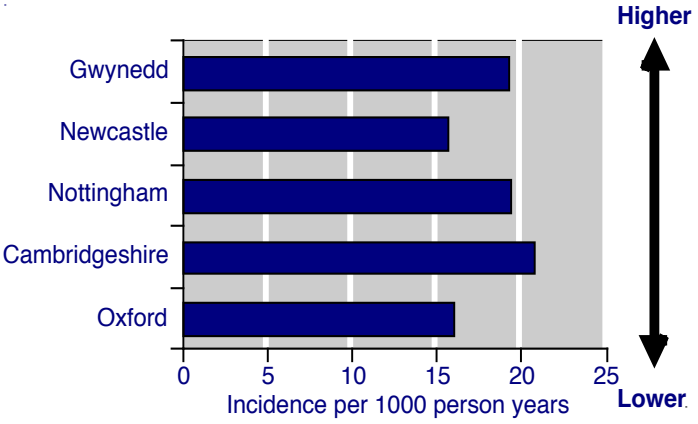
The findings have implications for planning of health services in the face of substantial increases of older people in the population now, and in the future, as well as the increasing proportion of older people in the population. It has interesting societal overtones as well, especially when newer prevention trials have only moderate preventative effects, with NNTs of about 90 over three years to prevent one case of cognitive impairment [2].

Reference:

1 F Matthews et al. The incidence of dementia in England and Wales: findings from the five identical sites of the MRC CFA study. PLoS Medicine 2005 2: e193.

2 K Yaffe et al. Effect of raloxifene on prevention of dementia and cognitive impairment in older women: the multiple outcomes of raloxifene evaluation (MORE) randomised trial. American Journal of Psychiatry 2005 162: 683-690.

Figure 2: Overall incidence of dementia in persons over 65 years in five UK areas with very different levels of vascular risk factors



High-risk mini strokes

A transient ischaemic attack (TIA) is usually defined as causing symptoms for less than 24 hours, but it is unlikely that brain or eye is actually ischaemic for more than a few minutes. What we observe is the clinical effects of reversible impairment of neuronal function resulting from a short period of ischaemia. The risk of stroke after a TIA is about 12% in the first year and then about 7% a year thereafter, with risk of stroke, heart attack or vascular death being about 10% a year. This is about seven times the risk in the background population. But there is also a high risk of stroke in the seven days after a TIA, possibly as high as 10%.

Although patients with a suspect TIA should be assessed and investigated within a week, this is often not achieved in practice. The problem may be deciding not what sort of care is most appropriate, but which patient having a TIA needs emergency assessment? A simple diagnostic scoring system [1] looks like being a real help.

Study

The likelihood of chance associations related to TIA and subsequent seven-day stroke was eliminated by using only factors previously significantly found to be independent predictors of stroke in the three months after a TIA. These were age, clinical features characterised (motor weakness and speech disturbance), duration of symptoms, diabetes, and hypertension. The criteria decided upon were:

- Age was dichotomised at 60 years.
- Hypertension was defined as elevated blood pressure after the TIA, with cut off points of 140 mmHg systolic and/or 90 mmHg diastolic.
- Motor weakness was focal, usually unilateral, weakness (loss of power) of face, arm, hand, or leg.
- Speech disturbance was dysarthria (impairment of articulation) or dysphasia (difficulty in speaking or understanding language), or both.
- Duration of symptoms was characterised as less than 10 minutes, between 10 minutes and 59 minutes, or 60 minutes or more.
- Diabetes was defined as treatment with oral medication or insulin.

These characteristics were tested on a derivation data set, a scoring system established (Table 1), and the scoring system tested on a validation data set. The derivation and validation data used information from several large population-based cohort studies performed in Oxford over several years. Two main studies each had about 100,000 people, with high levels of case ascertainment, and of follow up.

Results

The derivation dataset had 209 probable or definite TIAs and the validation dataset 190. Based on the derivation dataset in which diabetes was eliminated, and high levels of significance were found for unilateral weakness and duration of symptoms of 60 minutes or more, the ABCD scoring system was developed (Table 1).

Table 1: ABCD scoring system

ABCD	Meaning	Question	Score
A	Age	<60 years	0
		≥60 years	1
B	Blood pressure	Systolic >140 mmHg and/or diastolic ≥90 mmHg	1
C	Clinical features	Unilateral weakness	2
		Speech disturbance without weakness	1
		Other	0
D	Duration of symptoms	≥60 minutes	2
		10-59 minutes	1
		<10 minutes	0

This was tested on the validation data set, where 19/20 strokes occurring in the seven days after TIA had ABCD scores of 5 or 6 (Figure 1). In the 80 patients with ABCD scores of 5 or 6 there were 19 strokes within seven days of the TIA (24%, or 1 in 4). In patients with a score of less than 5, the seven day risk was 0.4%, or 1 in 250.

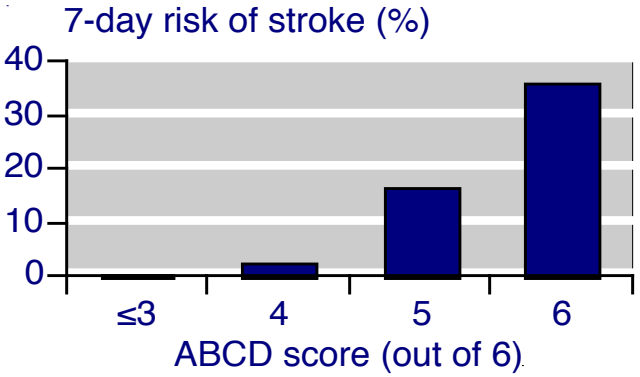
All of the strokes within seven days occurred in people with focal weakness or speech disturbance, and 16/20 had focal weakness. Focal weakness or speech disturbance, being older than 60 years, or duration of symptoms of 60 minutes or more captured 18 of 20 strokes.

Comment

This is a beautiful example of how to create and test a simple clinical scoring system. It used good quality derivation and validation data. There is much more to this study than Bandolier can capture, and, though detailed, it is one of those must-read papers. It will be useful to GPs, nurses, and emergency room staff to identify high risk of stroke after TIA, and to make appropriate decisions about how and where to care for such patients. Best of all, it provides a simple way for anyone to use some simple observations to judge the need for urgent hospital referral after a TIA.

Reference:
1 PM Rothwell et al. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. Lancet 2005 366: 29-36.

Figure 1: Results of scoring



Hormones, thrombophilia, and VTE

The use of oral contraceptives and hormone replacement therapy is associated with increased risk of venous thromboembolism (deep vein thrombosis or pulmonary embolism). Thrombophilia is the propensity to develop thrombosis (blood clots) due to an abnormality in the system of coagulation. One might expect, therefore, that there would be an even higher risk of venous thromboembolism in women who both had a thrombophilia and who took oral contraceptives or hormone replacement therapy. A systematic review [1] confirms that.

Systematic review

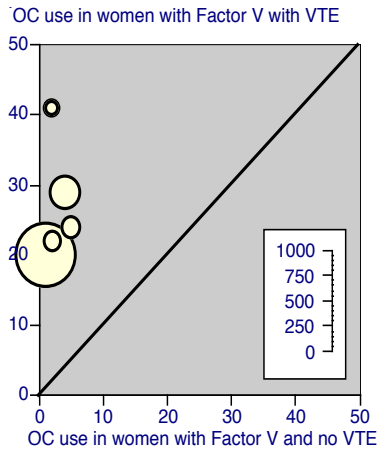
The review performed some heroic searching to find prospective or retrospective studies in which the study population included women using oral contraceptives or hormone replacement therapy. Clinical outcomes that included incidence of venous thromboembolism or mortality had to be reported, with information on the presence or absence of any thromboembolic defect.

Results

For oral contraceptive use, seven studies were found, predominantly case-control studies comparing women with a venous thromboembolism event (VTE) with control women. The rate of oral contraceptive use in women with VTE events (61%) was about double that with controls (29%; Table 1).

In women ***not*** taking oral contraceptives, the incidence of known thrombophilias was higher in those with a VTE. For factor V Leiden, where there were most data, the relative risk was 3.5 (95% CI 2.5 to 4.9). In women who had a VTE, use of oral contraceptive in the presence of Factor V Leiden occurred about 12 times more frequently than in control women who had not experienced a VTE (Figure 1). The relative risk was 12 (7.9 to 19). Although information for other thrombophilias was limited to information from only one or two trials, much higher risks were also seen for Prothrombin G20210A, antithrombin, protein C, and protein S deficiencies, and high levels of FVIIIc.

Figure 1: Use of OC with Factor V Leiden in women with and without VTE



There was only limited information for use of hormone replacement therapy and thrombophilia, but the results from two case-control studies was consistent with that from oral contraceptive use (Table 1).

Comment

The combination of oral hormone therapy together with an abnormality of coagulation is a bad thing. For oral contraceptives and factor V Leiden, the sum of the individual risks (5.5) was lower than the risk of the combined factors (12), and lower even than the lower confidence interval (7.9; Table 1). It may well be that the effect is supra additive.

Clearly oral contraceptives and hormone replacement therapy should be avoided in women with known defects in coagulation, but few women know whether they have or do not have these defects. Screening before use does not seem sensible, given the many different thrombophilias, and their low absolute incidence.

However, given the high incidence of thrombophilias in women who have had a thromboembolic episode (about 1 in 5 for Factor V Leiden alone), avoiding hormone therapy in these women would seem sensible.

Reference:

1 A Wu et al. Oral contraceptives, hormone replacement therapy, thrombophilias and risk of venous thromboembolism: a systematic review. Thrombosis and Haemostasis 2005 94: 17-25.

Table 1: Results for association of venous thromboembolism with oral contraceptive or hormone replacement use, Factor V Leiden, or both

Factor	Number of		Percent with factor in		Relative risk (95%CI)
	Studies	Patients	Had VTE events	Had no VTE events	
Oral contraceptive use	7	2530	61	29	2.0 (1.8 to 2.2)
Factor V Leiden, no OC	6	1617	19	6	3.5 (2.5 to 4.9)
Oral contraceptive and Factor V Leiden	6	1612	27	2	12 (7.9 to 19)
Hormone replacement therapy	2	359	62	38	1.7 (1.4 to 2.1)
Factor V Leiden, no HRT	2	221	21	7	3.1 (1.4 to 6.7)
HRT and Factor V Leiden	2	218	27	3	9.2 (3.5 to 24)

Book reviews

Evidence-based medicine and the search for a science of clinical care. Jeanne Daly. University of California Press. ISBN 0-520-24316-1. £41.95, US$ 65.00. 275pp.

We stand on the shoulders of others, and it is occasionally useful to meet and try to understand those whose shoulders we stand upon. Evidence-based medicine, or clinical epidemiology, or whatever you prefer to call it, did not spring fully into being overnight. Like all developments from pottery, writing, or cultivation of grain, it was a gradual development in which people learned what others had achieved, and improved upon it.

Jeanne Daly, herself no mean researcher and writer, has traced the stories and motivations of how EBM as we know it today has evolved, through interviews with many of the key contributors from the 1960s onwards. She gives us a series of their histories, and of their motivations and interactions. It is, like any such book, a personal account, but there is no harm in that.

Even when you know some of the players, and were around when some of the events and developments were occurring, you know only part of it. This book tells more. It is interesting to see coming though just how much the key players were, well, slightly maverick, in the good sense of somebody holding independent views, and refusing to conform to the accepted or orthodox thinking. Perhaps like most change, people had to think outside the box, and made sure that it wasn't just that the box was very small.

Difficulties had to be overcome. New thinking met with old certainties, and nobody likes some maverick coming along and suggesting some more detailed and insightful thinking about those certainties. Yesterday is just like today, and history isn't dead.

The cost is a bit steep for this to be light holiday reading, but borrow it, come to know just a little bit more, and who knows, be tempted to get out of the box yourself. This book should be read by anyone who wants to consider themseves expert on EBM, and those pontificating about it. The founders questioned, and kept on questioning. This is a lesson that needs eternally relearning.

Evidence-based to value-based medicine. MM Brown, GC Brown, S Sharma. American Medical Association Press. ISBN 1-57947-625-2. £52.25. 339pp.

Right at the end of this book, a final thought is that value-based medicine equals improved quality of care plus efficient use of healthcare resources. That seems fair enough, but actually this book is all about cost utility or cost effectiveness analysis, the resources expended for some improvement in life duration, or quality, or a combination, as in cost per QALY.

There's nothing wrong in that, and indeed, much right. Cost utility enables us to spend what resources we have in the most efficient way – or it would if budgets, politics, practice, and the difficulties in making change in large organisations did not intervene to complicate matters.

Getting a grip on cost utility is something that would benefit all of us, and this book helps. It details, for instance, a whole series of quality of life instruments, both general and specific. Looking at the actual measures used is rather interesting.

Figuring out discounting also clears a few cobwebs, and the table showing effects of discounting at different rates tells us that the time to reach half value is 70 years at 1%, 24 years at 3%, 15 years at 5%, but only eight years at 10%.

The problem, though, is that the book is more about economics than evidence, and what it says about evidence is uncritical. The format will irritate some, and the purely US perspective others. The problem is knowing who this book is for at this high price. It is too detailed and expensive for the general reader, but will be useful for those who want to get their brains firmly around cost utility.

Sexual health and the menopause. Ed JM Tomlinson. Royal Society of Medicine Press. ISBN 1-85315-620-5. £12.95. pp80.

Half of married women aged 66-71 are sexually active, almost a third of those aged over 78 years are sexually active, and the average frequency of sexual activity of people over 50 years in the USA is two to four times a month. Put that together with increasing divorce, more frequent or changing partners in older people, more older people, increasing rates of sexually transmitted infections in older people, and the need for a little book on sexual health in older people is obvious.

Though this book is headlined as being about the menopause, it is wider than that. It has 10 short and punchy chapters, including discussions on female and male sexual function and dysfunction. It includes good practical advice throughout, with one specifically on taking a sexual history.

The style is simple and the book is both readable and worth reading. Probably most useful in general practice, but not without value for us ordinary folk.

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